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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/596,516	JONES, WALTER KEITH
	Examiner	Art Unit
	WU-CHENG SHEN	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 19-33* is/are pending in the application.

4a) Of the above claim(s) *1,3,8-17 and 19-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4-7,32 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☐ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

This application 10/596,516 is a 371 of PCT/US2004/042950 filed on 12/20/2004 which claims benefit of 60/531,399 filed on 12/19/2003 and claims benefit of 60/574,131 filed on 05/25/2004.

Election/Restriction

In response to requirement for election of species mailed on 03/23/2011, Applicant's election with traverse of (I) wherein the domain is NF-kB specific (recited in claim 6), and (II) wherein the concatemerized double- stranded oligonucleotide molecule comprises at least 15 end-to-end repeated copies of a domain (recited in claim 32), in the reply filed on 04/18/2011 is acknowledged. The traversal is on the ground(s) that (I) A transcription factor decoy can be comprised of repeated domains that are from about 14 to about 40 (or from about 12 to about 25) nucleotide base pairs in length, wherein the domains are also NF-kB specific. Further, there is overlap between the ranges of nucleotide base pairs recited in claims 30 and 31. (II) a concatemerized double-stranded oligonucleotide molecule comprising at least 20 end-to-end repeated copies of a domain (claim 33) encompasses a concatemerized double-stranded oligonucleotide molecule comprising at least 15 end-to-end repeated copies of a domain (claim 32). This is not found persuasive because (I) claims 6, 30 and 31 are all depend from claim 2, different transcription factors (e.g. limitations recited in claim 7) bind distinct nucleotide sequences/domain, and the consensus nucleotide sequences/domain specifically bind NF-kB is 10 nucleotides (See more elaboration in the prior art rejection), which is not 14-40 nucleotides (recited in claim 30) or 12-25 nucleotides (recited in claim 31). Accordingly, claims 30 and 31 are directed to non-elected species. Nevertheless, with regard to (II) aspect of traversal, the

requirement for species election between the limitation recited in claims 32 and 33 is *withdrawn* upon further consideration. More elaboration in this regard is provided in the prior art rejection documented in this office action.

It has been documented on page 5 of the Election/Restrictions mailed on 03/23/2011 that upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

Claim 18 is cancelled. Claims 30-34 are newly added. Claims 1-17 and 19-33 are pending in the instant application. Claims 2 and 6 are amended.

Claims 1, 3, 8-17, and 19-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claims 2, 4-7, 32 and 33 are currently under examination to the extent of elected species (i.e. domain being NF-kB specific recited in claim 6 and NF-kB transcription factor recited in claim 7).

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejection - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

1. Previous rejection of claims 2 and 4-7 under 35 U.S.C. 102(a) and under 102(e) as being anticipated by **Dzau et al.** (US 2003/0186922, publication date 10/02/2003, filed on 04/25/2003, priority date 10/29/1993) is ***withdrawn*** because the claims have been amended.

Amended claim 2 filed on 01/26/2011 reads as follows: A transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule, wherein the concatemerized double-stranded oligonucleotide molecule comprises comprising at least 10 end-to-end repeated copies of a domain, wherein each of said domains comprises comprising a nucleotide sequence that acts as a transcription factor decoy for a transcription factor, and wherein each of said domains comprises from about 10 to about 40 nucleotide base pairs.

2. Claims 2, 4, 5, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by **Weintraub et al.** (Weintraub et al. Retinoblastoma protein switches the E2F site from positive to negative element, *Nature* 358(6383):259-61, 1992) is ***withdrawn*** because the claims have been amended.

Amended claim 2 filed on 01/26/2011 reads as follows: A transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule, wherein the concatemerized double-stranded oligonucleotide molecule comprises comprising at least 10 end-to-end repeated copies of a domain, wherein each of said domains comprises comprising a nucleotide sequence that acts as a transcription factor decoy for a transcription factor, and wherein each of said domains comprises from about 10 to about 40 nucleotide base pairs.

Claim Rejection - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 2 and 6 are ejected under 35 U.S.C. 103(a) as being unpatentable over **Weintraub et al.** (Weintraub et al. Retinoblastoma protein switches the E2F site from positive to negative element, *Nature* 358(6383):259-61, 1992) in view of **Sharma et al.** (Sharma et al. Transcription factor decoy approach to decipher the role of NF-kappaB in oncogenesis, *Anticancer Research*, 16(1): 61-69, 1996) is ***withdrawn*** because the claims have been amended.

Amended claim 2 filed on 01/26/2011 reads as follows: A transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule, wherein the concatemerized double-stranded oligonucleotide molecule comprises comprising at least 10 end-to-end repeated copies of a domain, wherein each of said domains comprises comprising a nucleotide sequence that acts as a transcription factor decoy for a transcription factor, and wherein each of said domains comprises from about 10 to about 40 nucleotide base pairs.

The following 103(a) rejection is necessitated by claim amendments filed on 01/26/2011.

4. Claims 2, 4-7, 32 and 33 are ejected under 35 U.S.C. 103(a) as being unpatentable over **Sharma et al.** (Sharma et al. Transcription factor decoy approach to decipher the role of NF-kappaB in oncogenesis, *Anticancer Research*, 16(1): 61-69, 1996) in view of **Dzau et al.** (US

2003/0186922, publication date 10/02/2003, filed on 04/25/2003, priority date 10/29/1993) and **Weintraub et al.** (Weintraub et al. Retinoblastoma protein switches the E2F site from positive to negative element, *Nature* 358(6383):259-61, 1992)

Claim 2 is directed to a transcription factor decoy comprising a concatemerized double-stranded oligonucleotide molecule, wherein the concatemerized double-stranded oligonucleotide molecule comprises comprising at least 10 end-to-end repeated copies of a domain, wherein each of said domains comprises comprising a nucleotide sequence that acts as a transcription factor decoy for a transcription factor, and wherein each of said domains comprises from about 10 to about 40 nucleotide base pairs.

Claim 4 is directed to the transcription factor decoy of claim 2, further comprising at least one tissue-specific promoter.

Claim 5 is directed to the transcription factor decoy of claim 2, wherein the transcription factor decoy is capable of blocking signaling and gene expression associated with pathogenesis.

Claim 6 is directed to the transcription factor decoy of claim 1, wherein the decoys are NF-κB-specific.

Claim 7 is directed to the transcription factor decoy of claim 2, wherein the transcription factor is selected from NF-kB.

Claim 32 is directed to the transcription factor decoy of claim 2, wherein the concatemerized double-stranded oligonucleotide molecule comprises at least 15 end-to-end repeated copies of a domain.

Claim 33 is directed to the transcription factor decoy of claim 2, wherein the concatemerized double-stranded oligonucleotide molecule comprises at least 20 end-to-end repeated copies of a domain.

With regard to the limitations of claims 2, 5, 6 and 7, **Sharma et al.** teaches that the NF-kB transcription factor complex participate in the induction of numerous cellular and viral genes, and the role of NF-kB in *oncogenesis* (See introduction and title). Sharma et al. teaches transcription factor decoy approach to decipher the role of NF-kappaB in oncogenesis. In an

effort to decipher the role of homo- vs heterodimeric NNF-kappa B in regulating tumor cell growth, Sharma et al. used a decoy approach to trap these complexes *in vivo*. Using *double-stranded phosphorothioates* as a direct *in vivo* competitor for homo- vs heterodimeric NF-kappa B, Sharma et al. demonstrate that decoys more specific to RelA inhibit growth tumor cell growth *in vitro*. Sharma et al. demonstrate that RelA, either as a homodimer or a heterodimer with some other members of the Rel family and not the classical NF-kB (RelA/NFKB1), is involved in the differential growth control of tumor cells (See abstract, Sharma et al., 1996). Sharma et al. further teaches that basis of transcription factor decoy (TFD) approach to inhibit transcription factor function *in vivo* (See Figure 1, shown below).

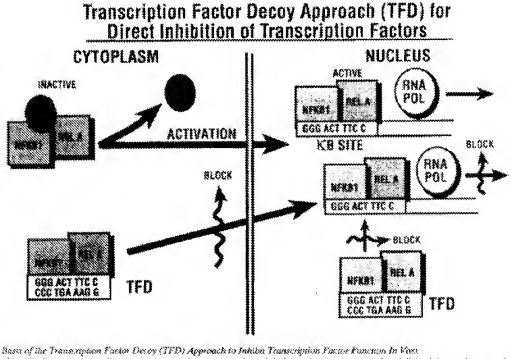


Figure 1. The Basis of the Transcription Factor Decoy (TFD) Approach to Inhibit Transcription Factor Function In Vivo.
Activation of the NF-κB transcription factor complex results in removal of IκB from the inactive complex, followed by nuclear translocation and transcriptional activation (left panel). In the presence of a TFD in the cytoplasm, the NF-κB complex can be sequestered by TFD prior to translocation, thus preventing nuclear translocation. A TFD in the nucleus can also bind to the active NF-κB complex, acting as a competitive inhibitor to block binding to cognate κB sites, thereby inhibiting transcription.

Sharma et al. teaches annealing the complementary stands *in vitro* in an annealing buffer to the NF-kB TFD sequences as follows:

5' GGG GAC TTT CCG CTG GGG ACT TTC CAG GGG GAC TTT CC 3'

It is noted that double-standed NF-kB TFD comprising ***three*** end-to-end repeated copies of consensus NF-kB binding site (5' GGG GAC TTT C 3'), which is 10 nucleotide base pairs.

Sharma et al. does not explicitly teach the limitations **(i)** "10 end-end repeated copies" recited in claim 2, "15 end-end repeated copies" recited in claim 32, and "20 end-end repeated copies" recited in claim 33, and **(ii)** further comprising at least one tissue-specific promoter recited in claim 4.

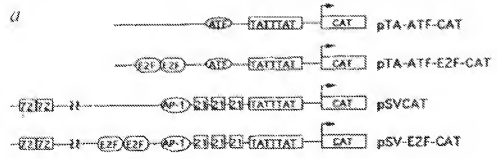
With regard to the limitations **(i)** "10 end-end repeated copies" recited in claim 2, "15 end-end repeated copies" recited in claim 32, and "20 end-end repeated copies" recited in claim 32, **Dzau et al.** teaches the use of oligodeoxynucleotide decoys for the prophylactic or therapeutic treatment of diseases associated with the binding of endogenous transcription factors to genes involved in cell growth, differentiation and signaling or to viral genes. By inhibiting endogenous trans-activating factors from binding transcription regulatory regions, the decoys modulate gene expression and thereby regulating pathological processes including inflammation, intimal hyperplasia, angiogenesis, neoplasia, immune responses and viral infection (See abstract, Dzau et al., 2003). Dzau et al. further teaches that the decoys contain sufficient nucleotide sequence to ensure target transcription factor binding specificity and affinity sufficient for therapeutic effectiveness. For the most part, the target transcription factors will require at least six base pairs, usually at least about eight base pairs for sufficient binding specificity and affinity. Frequently, providing the decoys with flanking sequences (ranging from about 5 to 50

bp) beside the binding site enhance binding affinity and/or specificity. Accordingly, *cis element flanking regions may be present and concatemer oligonucleotides may be constructed with* ***serial repetitions of the binding and/or cis element*** *flanking sequences* (See paragraph [0020], Dzau et al., 2003).

With regard to the limitation **(ii)** further comprising at least one tissue-specific promoter recited in claim 4, **Dzau et al.** teaches that the decoys may comprise a portion of a larger plasmid, including viral vectors, capable of episomal maintenance or constitutive replication in the target cell to provide longer term or enhanced intracellular exposure to the decoy sequence. Plasmids comprising *promoter* that regulates the expresses transcription factor decoy of interest are selected based on compatibility with the target cell (i.e. tissue specificity), size and restriction sites, replicative frequency, copy number maintenance, etc. For example, plasmids with relatively short half-lives in the target cell are preferred in situations where it is desirable to maintain therapeutic transcriptional modulation for less than the lifetime of the target cell (See paragraph [0021], Dzau et al., 2003).

Furthermore, **Weintraub et al.** teaches that the role of the E2F protein in *E1a* promoter activity was examined in transfection assays in which a competitor plasmid containing E2F binding sites was cotransfected with the plasmid pE1aCAT, which contains the E1a promoter fused to the gene for chloramphenicol acetyltransferase (*CAT*). This competitive binds and sequesters E2F, thus preventing it from interacting with the *E1a* promoter (See left column, page 259, Weintraub et al., 1992).

The diagram of the plasmids taught by Weintraub et al. in Figure 2a is shown below.



It is noted that there are multiple end-to-end transcription factor binding sites present in the promoter of double-stranded plasmid pTA-ATF-E2F-CAT and plasmid pSV-E2F-CAT.

Based on the combined teachings of Sharma et al., Dzau et al. and Weintraub et al., the ranges of the number of end-to-end repeats present in a NF-kB transcription factor decoy depend on the given cellular and viral genes to be inhibited in a given tissue in a desired *in vitro* experimental setting and/or intended *in vivo* therapeutic setting. The determination of the ranges of the number of end-to-end serial repeats present in a NF-kB transcription factor decoy is a process of optimization.

2144.05 [R-5] Obviousness of Ranges

See MPEP § 2131.03 for case law pertaining to rejections based on the anticipation of ranges under 35 U.S.C. 102 and 35 U.S.C. 102/103.

II. OPTIMIZATION OF RANGES

A. Optimization Within Prior Art Conditions or Through Routine Experimentation

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie

obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.). For more recent cases applying this principle, see Merck & Co. Inc. v. Biocraft Laboratories Inc., 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989); In re Kulling, 897 F.2d 1147, 14 USPQ2d 1056 (Fed. Cir. 1990); and In re Geisler, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997).

B. Only Result-Effective Variables Can Be Optimized

A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq. ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable.). See also In re Boesch, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) (prior art suggested proportional balancing to achieve desired results in the formation of an alloy).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time of the invention to combine the teachings of Sharma et al. regarding the NF-kB transcription factor complex participate in the induction of numerous cellular and viral genes, and the role of NF-kB in oncogenesis, transcription factor decoy approach to decipher the role of

NF-kappaB in oncogenesis, and the double-stranded NF-kB TFD comprising three end-to-end repeated copies of consensus NF-kB binding site (5' GGG GAC TTT C 3'), which is 10 nucleotide base pairs, with the teachings of **(i)** Dzau et al. regarding *cis* element flanking regions may be present and concatemer oligonucleotides may be constructed with ***serial repetitions*** of the binding and/or *cis* element flanking sequences, and the decoys may comprise a portion of a larger plasmid, including viral vectors, capable of episomal maintenance or constitutive replication in the target cell to provide longer term or enhanced intracellular exposure to the decoy sequence, and (ii) Weintraub et al. regarding the role of the E2F protein in *E1a* promoter activity was examined in transfection assays in which a competitor plasmid containing E2F binding sites was cotransfected with the plasmid pE1aCAT, which contains the E1a promoter fused to the gene for chloramphenicol acetyltransferase (*CAT*), to arrive at claimed transcription factor decoy recited in claims 2, 4-7, 32 and 33 of instant application

One having ordinary skill in the art would have been motivated to combine the teachings of Sharma et al. with the teachings of Dzau et al., and Weintraub et al. because Sharma et al. teaches a functional role of NF-κB transcription factor in regulation of oncogenes is and using double-stranded NF-kB TFD comprising **three** end-to-end repeated copies of consensus NF-kB binding site (5' GGG GAC TTT C 3') whereas Dzau et al. specifically teaches that *cis* element flanking regions may be present and concatemer oligonucleotides may be constructed with ***serial repetitions*** of the binding and/or *cis* element flanking sequences, and Weintraub et al. teaches an example of promoter designed for analysis of retinoblastoma (RB) protein regulating E2F transcription factor binding to multiple E2F sites.

There would have been a reasonable expectation of success given (i) the successful demonstration of transcription factor decoy approach to decipher the role of homo- vs heterodimeric NNF-κB in regulating tumor cell growth, by the teachings of Sharma et al., (ii) successful demonstration of effect of decoy ODN (oligodeoxynucleotides) on *in vitro* and *in vivo* gene expression (See Examples 1-3), by the teachings of Dzau et al., and (iii) the successful demonstration of plasmids with multiple E2F transcription factor binding sites functioning as a transcription factor decoy that sequesters E2F transcription factor and thus preventing E2F transcription factor from interacting with the *E1a* promoter, by the teachings of Weintraub et al.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

The Examiner would like to direct Applicant's attention to recent decision by U.S. Supreme Court in *KSR International Co. v. Teleflex, Inc.* that forecloses the argument that a **specific** teaching, suggestion, or motivation is an absolute requirement to support a finding of obviousness. See recent Board decision *Ex parte Smith*, --USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing KSR, 82 USPQ2d at 1936) [available at http://www.uspto.gov/web/offices/dcom/bpai/prec/fd071925.pdf; and *KSR Guidelines Update* has been published in the Federal Register at 75 *Fed. Reg.* 53643-60 (Sep. 1, 2010) and is posted at USPTO's internet Web site at http://www.uspto.gov/patents/law/notices/2010.jsp]. The Examiner notes that in the instant case, even in the absence of recent decision by U.S. Supreme Court in *KSR International Co. v. Teleflex, Inc.,* the suggestion and motivation to combine the teachings of Sharma et al. with the teachings of Dzau et al. and Weintraub et al. has been clearly set forth above in this office action.

It is noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant's arguments and ***Response to Applicant's arguments***

Applicant's remarks regarding the previous rejection of record are addressed as the related to the new grounds of rejection set forth above.

The Examiner acknowledges Applicant's arguments that "Although Dzau discloses the decoys of his invention may be constructed with serial repetitions of the binding sequences, Dzau is limited to comparatively short oligonucleotides "having fewer than 100 bp, and usually fewer than 50 bp." See paragraph [0021] of Dzau, emphasis added. The longest oligonucleotide disclosed in Dzau's working examples is a 30 bp oligonucleotide decoy having two 8 bp E2F cis elements. See paragraphs [0034]-[0038] of Dzau. Conversely, the instantly claimed transcription factor decoys are comparatively longer and comprise at least 10 repeated copies of a domain, each domain comprising about 10 to about 40 nucleotide bases." (See page 8 of Applicant's remarks filed on 01/26/2011)

For the clarity of record, the paragraphs [0020]-[0021] disclosed by Dzau et al. are cited below.

[0020] The decoys contain sufficient nucleotide sequence to ensure target transcription factor binding specificity and affinity sufficient for therapeutic effectiveness. For the most part, the target transcription factors will require at least six base pairs, usually at least about eight base pairs for sufficient binding specificity and affinity. Frequently, providing the decoys with flanking sequences (ranging from about 5 to 50 bp) beside the binding site enhance binding affinity and/or specificity. Accordingly, cis element flanking regions may be present and ***concatemer oligonucleotides may be constructed with serial repetitions of the binding and/or cis element flanking sequences.***

[0021] *In one embodiment*, the decoys are non-replicative oligonucleotides fewer than 100 bp, *usually* fewer than 50 bp and usually free of coding sequence, being primarily from the non-coding 5' region of a gene. Alternatively, the decoys may comprise a portion of a larger

plasmid, including viral vectors, capable of episomal maintenance or constitutive replication in the target cell to provide longer term or enhanced intracellular exposure to the decoy sequence. Plasmids are selected based on compatibility with the target cell, size and restriction sites, replicative frequency, copy number maintenance, etc. For example, plasmids with relatively short half-lives in the target cell are preferred in situations where it is desirable to maintain therapeutic transcriptional modulation for less than the lifetime of the target cell. Exemplary plasmids include pUC expression vectors driven by a beta-actin promoter and CMV enhancer, vectors containing elements derived from RSV or SV40 enhancers, etc. The adeno-associated viral vector preferentially integrates in chromosome 19 and may be utilized for longer term expression.

The Examiner notes that from the context of the paragraphs [0020]-[0021] disclosed by Dzau et al., it is clear that Dzau et al. discloses multiple embodiments of the designs of transcriptional factor decoy. The embodiment disclosed in paragraph [0020] does not in any way "*limit*" the transcription factor decoy to comparatively short oligonucleotides "having fewer than 100 bp, and usually fewer than 50 bp", as Applicant asserts, in the context of the embodiment disclosed in paragraphs [0020]-[0021] of Dzau et al. Furthermore, the breadth of claims 2, 32 and 33 regarding at least 10 (15 or 20) end-to-end repeats encompasses (i) embodiment of chemically synthesized double-stranded TFD, and (ii) embodiment of double-stranded TFD comprising a promoter in the context of an expression vector (claim 4 of instant application). Accordingly, the breadth of claims 2, 32 and 33 regarding at least 10 (15 or 20) end-to-end repeats clearly encompasses the disclosure of paragraphs [0020] and [0021] by Dzau et al.

Therefore, as stated in the 103(a) rejection documented in this office action, based on the combined teachings of Sharma et al., Dzau et al. and Weintraub et al., the ranges of the number of end-to-end repeats present in a NF-kB transcription factor decoy depend on the given cellular and viral genes to be inhibited in a given tissue in a desired *in vitro* experimental setting and/or intended *in vivo* therapeutic setting. The determination of the ranges of the number of end-to-end serial repeats present in a NF-kB transcription factor decoy is a process of optimization.

Conclusion

5. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication from the examiner should be directed to Wu-Cheng Winston Shen whose telephone number is (571) 272-3157 and Fax number is 571-273-3157. The examiner can normally be reached on Monday through Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the supervisory patent

examiner, Peter Paras, Jr. can be reached on (571) 272-4517. The fax number for TC 1600 is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Wu-Cheng Winston Shen/
Primary Examiner
Art Unit 1632